Debridement, antibiotics and implant retention for periprosthetic joint infections: A systematic review and meta-analysis of treatment outcomes

Running Title: DAIR for periprosthetic joint infections

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Summary

Objectives: We aimed to assess infection control rates after DAIR in patients with periprosthetic joint infection (PJI) following joint arthroplasty and evaluate factors associated with infection control using a systematic review and meta-analysis.

Methods: We searched MEDLINE, EMBASE, Web of Science, Cochrane databases and reference lists of relevant studies up to May 2017. Longitudinal studies conducted in patients with PJI treated exclusively by DAIR were eligible. Infection control rates were meta-analysed using random-effect models after arcsine transformation.

Results: We included 93 articles based on 99 unique observational studies with data on 4897 PJIs treated by DAIR. The infection control rate for DAIR ranged from 11.1% to 100% with an overall pooled estimate of 61.4% (95% CI, 57.3-65.4) and a 95% prediction interval of 25.5 to 91.8%. Infection control rates remained generally similar for several relevant characteristics, except for evidence of variation by age, geographical location, type of infection and joint affected, duration of parenteral antibiotic therapy after the DAIR procedure, and period (year) of DAIR procedure.

Conclusions: The DAIR approach remains an option for the treatment of PJI as it is associated with acceptable infection control rates, particularly in acute postoperative infections and infections of the hip and shoulder joints.

Systematic review registration: PROSPERO 2017: CRD 42017057513

Key words: periprosthetic joint infection; total joint arthroplasty; debridement, antibiotics and implant retention; infection control; systematic review, meta-analysis

Introduction

Total joint arthroplasty, which is one of the most common surgical procedures, is an effective intervention for alleviating the pain and disability associated with advanced joint disease.(1-4) The numbers of total joint arthroplasties is projected to increase,(5-7) as a result of increasing life expectancy and a subsequently growing healthcare burden due to osteoarthritis and other joint conditions associated with ageing.(8) Periprosthetic joint infections (PJIs) though uncommon, are serious and devastating complications of total joint arthroplasties.(9, 10) Periprosthetic joint infections have major negative effects on patients' quality of life(11-13) and can result in severe pain, impaired function, and even death if left untreated.(14) Treatment options for PJI include long-term suppressive antibiotic treatment which is generally reserved for patients who are not suitable for surgery due to comorbidities;(15) debridement, antibiotics and implant retention (DAIR); one- or two-stage revision; and resection arthroplasty. Arthrodesis or amputation is normally considered as a last resort.(16, 17) In the management of PJI, the immediate and long-term goals include the control of infection, preventing recurrence, minimizing morbidity, pain relief, and optimizing joint function.(18-21) For the treatment of chronic PJI, most individuals undergo revision surgery with one or two operations. In the more widely used two-stage revision, prosthetic components are removed with extensive debridement of infected tissue and delayed re-implantation of revision components after a period of antibiotic therapy with no prosthesis in situ or a temporary spacer or implant. Although widely used, the two-stage strategy involves two extensive surgical procedure and is frequently associated with prolonged hospitalisation, significant functional impairment, and morbidity.(22) Thus, surgical revision using a one-stage strategy, with removal of prosthetic components, debridement and implant replacement in a single operation, is increasingly being used.(23, 24) For some patients, DAIR is considered as an alternative option, as it involves a less extensive surgical procedure and is associated with a shorter hospital stay, improved joint function, and less morbidity.(20, 25)

The DAIR approach has been recommended for the treatment of early PJIs.(26-29) Despite published evidence and guidelines on the treatment of PJI using DAIR, its role and appropriateness in the treatment of PJI still remain controversial, as the evidence and recommendations are mostly based on non-randomised observational studies, case series, and/or expert opinion. Infection control rates of DAIR for hip and knee PJI varies in the literature and have been reported to range from as low as 0% to as high as 100%.(30, 31) A number of factors have also been reported to influence the success rates of DAIR, some of which include the type of infecting micro-organism, duration of symptoms, length of antibiotic use, and the period between the onset of symptoms and initiation of treatment.(32-35) The results of previous studies have been inconsistent and studies were often poorly powered to adequately quantify the infection control rates and reliably evaluate potential factors that influence treatment outcomes of DAIR, were based on inadequate follow-up times, and cases were sometimes a mix of arthroplasties of different joints. A number of reviews have also been published in an effort to summarise the existing evidence. In a review of 23 studies which included 530 infected total knee arthroplasties treated using an open DAIR approach, Silva and colleagues reported infection control in 32.6% of the infected knees.(36) In the same review, 52.2% of 23 infected knees from four studies were free from infection after arthroscopic DAIR. In a narrative review of 52 studies of DAIR for infected total knee arthroplasty, the authors identified factors such as presence of a sinus, being immunocompromised, short antibiotic duration, and delay between onset of infection and debridement procedure, to be important contributors of failure to control infection.(28) In a review of 28 studies involving 599 cases of PJIs of the knee, the overall success rate after DAIR was reported to be 47%. Findings from this review suggested that the rate of infection remission was significantly higher in streptococcal knee PJIs compared with staphylococcal knee PJIs.(31) There were several features of these reviews which limited the validity of the findings. First, the majority of these reviews did not pool the evidence using appropriate meta-analytic methods, which should take into account the variability of the included studies. Second, none of the reviews explored for potential sources of heterogeneity among the contributing studies. Third, none of the reviews conducted any subgroup analysis across important study-level and clinically relevant characteristics (e.g. age at baseline, the type of infecting micro-organism, type of joint affected, length of antibiotic use, the period between the onset of symptoms and initiation of treatment, follow-up period, and methodological quality scores of included studies). Fourth, preferential publication bias was not assessed. In addition, several relevant individual reports have been published since the publication of these reviews.

With the current interest in the use of DAIR for treating PJI, there is a need for robust evidence on the effectiveness of the DAIR strategy in controlling PJI. In the absence of data from a carefully designed large-scale prospective study or randomised controlled trial (RCT); we aimed to use a systematic review and meta-analysis to (i) assess a reliable magnitude of the infection control rate after DAIR in patients with PJI following total joint arthroplasty and (ii) evaluate factors associated with infection control by assessing if infection control rates varied across several study-level and clinically relevant characteristics.

Methods

Data sources and search strategy

This review is registered in the PROSPERO prospective register of systematic reviews (CRD 42017057513), and was conducted in accordance with PRISMA and MOOSE guidelines(37, 38)(**Supplementary Materials 1-2**). We systematically searched MEDLINE, EMBASE, and Web of Science from inception up to May 2017. The computer-based searches combined free and MeSH search terms and combination of key words related to DAIR, PJI, and joint arthroplasty. The search was restricted to studies of humans. We complemented the search by manually scanning reference lists of key identified articles and review articles for relevant publications missed by the original search. Details on our search strategy are presented in **Supplementary Material 3**.

Eligibility criteria

We systematically searched for longitudinal studies (prospective or retrospective case control, prospective cohort, retrospective cohort, case-cohort, nested-case control, or clinical trials) that reported infection control following the use of DAIR in patients with PJI following total joint arthroplasty. A successful treatment outcome (infection control) was the primary endpoint of our review and this was defined by studies as no evidence of infection or eradication of infection based on clinical and laboratory confirmation or survival of the prosthesis in the absence of long-term antibiotic suppression or if patients did not undergo further revision procedures using other surgical procedures during the follow-up period. We excluded studies (i) that reported on patients who were treated by a variety of other surgical methods for the same infection at the same time; (ii) of any other surgical approach apart from total joint arthroplasty such as in the setting of fracture, hemiarthroplasty, or resurfacing arthroplasty; and (iii) that were restricted to patients who had undergone revision arthroplasty.

Data extraction and quality assessment

After the initial screen of titles and abstracts by one reviewer (S.K.K.), potentially relevant articles were acquired. Full texts of articles were assessed by two independent reviewers (S.K.K., A.D.B.) using the inclusion criteria. Any discrepancies regarding eligibility of an article were discussed, and consensus reached with a third author (M.R.W). One author (S.K.K.) independently extracted data and performed quality assessments using a standardized predesigned data collection form. A second reviewer checked extracted data with that in the original articles. In the case of multiple publications involving the same cohort, data were extracted from the most up-to-date study or study with the most comprehensive information was abstracted. When available, data were extracted on: publication date; study design; year of study/data collection; geographical location; mean or median age of patients; percentage of males; primary surgery; time from index surgery to onset of symptoms, diagnosis of PJI, and DAIR; duration of infection symptoms prior to DAIR; infection type (acute postoperative vs acute haematogenous vs late chronic); main pathogen involved; DAIR approach (arthroscopic vs open); duration of follow-up from DAIR; sample size (number of patients or PJIs); and infection control after DAIR. Methodological quality of included studies was assessed based on the Methodological Index for Non-Randomised Studies (MINORS), a validated instrument which is designed for assessment of methodological quality of non-randomized studies in surgery (39) and has been described previously.(40) Briefly, it uses eight pre-defined domains namely: a clearly stated aim; inclusion of consecutive patients; prospective collection of data; endpoints appropriate to the aim of the study; unbiased assessment of the study endpoint; follow-up period appropriate to the aim of the study; loss to follow-up less than 5%; and prospective calculation of the study size. For non-comparative studies, the total score ranges from 0 to 16 (worst to best quality).

Statistical analysis

The infection control rate (estimated from the number of infections successfully treated within follow-up period/total number of participants with PJI or PJIs as reported) with 95% confidence intervals (CIs) was used as the summary measure across studies. The Freeman-Tukey variance stabilising double arcsine transformation (41) was used in calculating the rates, because the use of the inverse variance weight in fixed-effects meta-analysis is suboptimal when dealing with binary data with low rates, as evidenced in our data.(40) To account for the effect of between-study heterogeneity anticipated, summary infection control rates were pooled using random effects models (42). We also estimated 95% prediction intervals which are used to determine the degree of heterogeneity, as they provide a region in which about 95% of the true effects of a new study are expected to be found.(43, 44) Standard chi-square tests and the I^2 statistic (45) were used to quantify the extent of statistical heterogeneity across studies. We assessed for heterogeneity by several study-level characteristics using stratified analysis and random effects meta-regression.(46) We also evaluated for publication bias using Egger's regression symmetry tests.(47) STATA release 14 (Stata Corp, College Station, Texas, USA) was used for all statistical analyses.

Results

Study identification and selection

Our search identified 2557 potentially relevant citations. After an initial screen based on titles and abstracts, we selected 157 articles for full text evaluation. Following detailed assessments, 64 articles were excluded because (i) they were duplicates or used the same population sample as other studies included in the review (n=22); (ii) the populations used were not relevant to review (n=20); (iii) the surgical interventions used were not relevant (n=8); (iv) they were conference publications (n=6); (v) outcomes were not relevant to review (n=5); or (vi) the study designs were not relevant (n=3). The remaining 93 articles based on 99 unique observational studies met all inclusion criteria and were included in the review (**Fig. 1; Supplementary Materials 4-5**).

Study characteristics and study quality

Table 1 provides a summary of baseline and clinical characteristics of studies included in the review. **Supplementary Material 5** summarizes the key characteristics and quality assessment scores of the individual studies. In aggregate, 4897 PJIs were included in the pooled analysis. Sample size of the studies ranged from 3 to 345 joints with PJIs. A total of 40 studies were conducted in North America (USA); 36 in Europe (Netherlands, Switzerland, Spain, Slovenia, UK, Finland, Norway, Denmark, Sweden, Italy, France, and Germany); 10 in Asia (Taiwan, Japan, South Korea, and China); six in the Pacific (Australia and New Zealand); and one in South America (Brazil). The mean or median baseline age of participants ranged from 55 to 80 years. All eligible studies were longitudinal observational studies and comprised of 82 retrospective and 11 prospective cohort designs. The average follow-up duration after DAIR ranged from 1.0 to 7.1 years. Methodological quality of included studies ranged from 10-14.

Infection control rate after DAIR

Across the 93 eligible studies comprising of 4897 PJI infections treated with DAIR, infection control rates ranged from 11.1% to 100%. The pooled random effects infection control rate (95% CI) was 61.4% (57.3-65.4; $p < 0.01$) (**Fig. 2**). The 95% prediction interval for the summary infection control rate was 25.5 to 91.8%, suggesting that the true infection control rate for any single new study will usually fall within this range. There was substantial heterogeneity between contributing studies (I^2=86%, 95% CI: 84-88%; $p < 0.01$), which was partly explained by geographical location, average baseline age, type of infection, type of joint affected, duration of parenteral antibiotic therapy after the DAIR procedure, and period of DAIR procedure (**Fig. 3**). In further exploration of heterogeneity, we restricted analyses to studies of hip and knee joints and this substantially reduced heterogeneity to (I^2=59%, 95% CI: 29-76%; $p < 0.01$). Among these studies, the pooled infection control rate (95% CI) was 75.4% (69.6-80.9; $p < 0.01$) with a 95% prediction interval of 54.4 to 91.9%.

Subgroup analyses

Except for statistically significant evidence of variation by geographical location (*p* for meta-regression<0.001), average baseline age (*p* for meta-regression=0.022), type of infection (acute vs chronic) (*p* for meta-regression=0.012), joint type (*p* for meta-regression<0.001), duration of parenteral antibiotic therapy after DAIR ((*p* for meta-regression=0.01), and period of DAIR procedure for all joint types (*p* for meta-regression=0.020), infection control rates were generally similar across several study relevant characteristics (**Fig. 3**). Infection control was higher in older individuals (≥ 70 years) compared to less older individuals (< 70 years). Higher infection control rates were observed in patient populations based in Europe, the Pacific, and South America compared with those in Asia and North America and in acute infections (acute postoperative and haematogenous) compared with late chronic infections. In subgroup analysis by joint type, DAIR was associated with higher infection control in hip, elbow, and shoulder joints compared with knee joints. Patients administered parenteral antibiotics for a period of ≤ 14 days after DAIR had higher infection control compared with those who received parenteral antibiotics for > 14 days. Infection control was higher for DAIRs conducted in the period 2000 and beyond compared to those conducted before the year 2000 in all joint types. However, in sub-analysis by joint type, there was no statistically significant evidence of any variations in infection control by period of DAIR procedure in both hip and knee infections. Recognising that infections occurring within two years of the intervention are mainly as a consequence of the surgical intervention,(48, 49) we also conducted subgroup analysis by follow-up period after DAIR (≤ 2 vs > 2 years) and we observed infection control rates to be similar across both groups (*p* for meta-regression = 0.602) (**Fig. 3**).

Publication bias

There was no statistically significant evidence of publication bias using the Egger test (*p*=0.858), which was consistent with the absence of selective reporting when studies were grouped by size (**Fig. 3**).

Discussion

Key findings

Given the uncertain role of DAIR and its appropriateness in the treatment of PJI, using a systematic and meta-analytical approach, we attempted to obtain a precise magnitude of infection control rates after DAIR in patients with PJI following joint arthroplasty and assess if infection control rates varied across several relevant clinical factors. We included data on 99 unique observational studies based on patients with PJI recruited from five continents. Based on individual study findings, infection control rates ranged from 11% to 100% and averaged approximately 61% in pooled analysis. When analysis was restricted to hip and knee joints, the average infection control rate was 75.4%. The infection control rates were generally similar across several study level and clinically relevant characteristics such as specific infecting organism, DAIR approach, duration of follow-up, methodological quality of studies, and period of DAIR procedure for hip and knee joints; except for evidence of variation by geographical location, age, infection type, joint type, duration of parenteral antibiotic therapy after DAIR, and period of DAIR procedure for all joint types. Infection control rates were higher in patient populations based in Europe, the Pacific, and South America compared with those in Asia and North America; in older patients compared with less older patients; in acute infections compared with late chronic infections; in hip, elbow, and shoulder joints compared with knee joints; in patients administered parenteral antibiotics for a period of 14 days and less after DAIR compared with those who received parenteral antibiotics for more than 14 days; and in patient populations who had a DAIR in 2000 and beyond compared to those who had the procedure before the year 2000.

Comparison with previous work and explanation of findings

Though a number of reviews have been conducted on the topic and our findings do overlap with some of these previous reports; our review provides several novel and relevant findings that have not been reported previously. By employing statistical approaches, our findings suggest that factors such as the geographical location, baseline age, type of infection, type of joint affected, duration of parenteral antibiotic therapy, and year in which DAIR was performed, may influence infection control after the procedure. Though a previous study found no substantial difference in infection control with DAIR comparing > 3 weeks with < 3 weeks duration of symptoms;(50) our results show that a longer duration between onset of symptoms to DAIR (≥ 21 days) is associated with lower infection control compared with a shorter duration (< 21 days), though the test of interaction was marginally significant. Our results concur with evidence which shows that the duration of symptoms is an important factor for successful infection control in DAIR(48, 51) along with previous recommendations that suggest a DAIR approach is likely to be successful for the treatment of early infections if the duration does not exceed three weeks.(48) The statistically nonsignificant result may indicate low power in the subgroup analysis. In a narrative review of 52 studies of DAIR for infected total knee arthroplasty, Qasim and colleagues suggested that factors such as presence of a sinus, compromised immunity, delay between onset of infection and debridement procedure, short antibiotic duration, and an open debridement procedure, to be important contributors of treatment failure.(28) Contrary to the findings of Qasim et al.,(28) we showed that shorter compared with longer parenteral antibiotic duration was associated with higher infection control. In our analysis by DAIR type, infection control rates were 60.3% and 71.8% for open and arthroscopic DAIR respectively, though the difference was not statistically significant. Silva and colleagues reported an infection control rate of 32.6% in a review of 23 studies including infected total knee arthroplasty treated with open DAIR; whilst in the same study, they reported an infection control rate of 52.2% in pooled analysis of four studies of infected knee arthroplasty treated with arthroscopic DAIR.(36) In a review of 28 studies of knee PJIs treated by DAIR, infection control averaged 47% and infection remission was higher for streptococcal compared with staphylococcal PJIs.(31) Findings from our analyses by specific infecting organism suggested similar infection control for Gram negative and Gram positive organisms and further analysis confirmed higher infection control for streptococcal infection (89.5%) compared with staphylococcal species (75.2%). Indeed, *Staphylococcus aureus* infection, particularly Methicillin-resistant *Staphylococcus aureus* (MRSA), has been shown to be associated with high failure rates after DAIR.(20, 52, 53) Consistent with the literature,(36, 54, 55) our findings confirmed higher infection control in acute postoperative infections compared with acute haematogenous and late chronic infections using the DAIR approach. Furthermore, our study findings demonstrated that when comparing the two most common joints, infection control was higher for infected hip arthroplasty (75.4%) compared with infected knee arthroplasty (52.6%). The finding of higher infection control with DAIR in European populations compared with North American populations, may reflect the fact that DAIR is more commonly used in Europe for treating PJI whilst a two-stage strategy is traditionally used in the USA.(50) The higher infection control rate observed in older individuals, may also reflect the fact that the elderly are less likely to be subjected to more invasive surgical procedures compared with less older individuals; and since some studies define treatment failure following DAIR as a further revision procedure using other surgical procedures, younger individuals are more likely to be reported as having a treatment failure compared with their older counterparts. Finally, we observed higher infection control for DAIRs done in the year 2000 and beyond compared to DAIRs performed in the 1980's and 1990's, perhaps reflecting improved surgical strategies and newer and more effective antimicrobial therapies in recent times. There was also a trend towards more favourable infection control rates for DAIR procedures in knee PJI performed in the year 2000 and beyond compared to those conducted before the year 2000. The significantly better infection control with a shorter duration of antibiotics following intervention may represent selection for these particular strategies on the basis of the severity of the presenting PJI or the adequacy of control of the PJI at the DAIR procedure.

Implications of our findings

The current findings provide further insight on infection control using the DAIR approach, which may have implications for the treatment of PJI. Overall, the findings do demonstrate that the DAIR procedure is an effective treatment option for the majority of PJIs. Although, in the majority of cases, DAIR is effective in treating PJI; one- and two-stage revision for infection following hip and knee replacement results in higher infection control rates. Systematic review and meta-analyses of data from cohort studies show infection eradication of 91.8% in one-stage revision for infected hip replacement, 92.1% in two-stage revision for infected hip replacement,(56) 92.4% in one-stage revision for infected knee replacement, and 91.2% in two-stage revision for infected knee replacement.(57) This higher rate of infection eradication needs to be balanced against the burden(11, 13) and risk of undergoing much more radical and invasive surgery. In the absence of RCTs comparing DAIR with revision surgery, it appears the results from aggregate data of cohort studies suggest inferior infection control rates compared to those achieved with one- or two-stage revision. However, DAIR is a far less invasive procedure and does not preclude subsequent revision surgery. It may be that an optimal treatment algorithm includes DAIR followed by implant revision in cases where the DAIR proves to be unsuccessful. DAIR has generally been the recommended treatment in patients with acute infections in a previously well-functioning prosthesis that is not loose, infections caused by low virulent organisms, and patients who are not immunocompromised.(58-60) Indeed, our findings showed that patients with acute postoperative infections had better infection control. Paradoxically, *Staphylococcus aureus* commonly accounts for most acute postoperative infections and are also associated with comparatively higher failure rates after DAIR. (20, 52, 53) Zurcher-Pfund et al. and others recommend that the implant should not be retained in MRSA infections in addition to established indications such as presence of a sinus tract as well as implant loosening.(28, 31) As observed in previous reports,(28) a delay between onset of infection and DAIR procedure is associated with low infection control, and should be taken into account when considering performing a DAIR. Though our findings do suggest a higher infection control rate for arthroscopic debridement when compared with open debridement, the results were not significantly different and the pooled infection control rate for arthroscopic DAIR was based on only few studies. Though DAIR is associated with good infection control in both hip and knee joints, the current evidence suggests that infection control rates are better for hip joints and this needs to be taken into account when selecting the most appropriate intervention for a particular joint. Our findings of higher infection control with shorter duration of parenteral antibiotic therapy may seem unexpected; however, this may be plausible as several studies have demonstrated no differences in infection control when comparing shorter duration with longer duration of antibiotics post-procedure(61, 62) and other studies have also shown that prolonged parenteral antibiotic therapy does not guarantee improved infection control.(35, 59, 63) Current guidelines suggest 4-6 weeks of pathogen-specific intravenous antimicrobial therapy.(29) Based on previous data(64) and our current findings, switching from parenteral to oral antibiotics at an early stage post-DAIR may be as effective as prolonged parenteral therapy if not more effective. Nevertheless, duration of parenteral antibiotics may also depend on the virulence of the infecting micro-organism and adequate bone penetration, which varies between antibiotics. Furthermore, there is a possibility that our findings may be due to selection bias, as duration of parenteral antibiotics also depend on response of PJI to treatment; antibiotics are stopped in patients who recover well, whereas parenteral antibiotics are continued in patients with persistent symptoms and/or signs of infection.

Study strengths and limitations

The current review has several strengths compared with previous reviews. To our knowledge, it is the most comprehensive and up to date assessment of the role of DAIR in treating PJIs. We implemented a search strategy across several databases as well as a manual scan of key relevant reviews on the topic, which yielded 93 published articles from five continents. Using a well-known validated instrument for non-randomised surgical studies, we conducted a detailed assessment of the methodological quality of the included studies. Unlike previous reviews, we employed a meta-analytic approach across studies, which yielded a pooled estimate of infection control. Furthermore, our approach took into account the heterogeneity between contributing studies and ensured that studies with zero rates were not excluded from the pooled analysis. We compared infection control among a broad range of study-level and clinically relevant characteristics. Our analysis suggested no significant difference in infection control rates between low- and high-quality studies. Finally, we quantified heterogeneity and explored for potential sources of bias, which included heterogeneity and small study effects. We found no evidence of publication bias. There were several limitations that deserve consideration. The majority of studies did not distinguish between primary and revision arthroplasty cases, therefore it is not possible to differentiate between the two in terms of infection control. The retrospective designs of the majority of included studies in this review introduces biases because of the risk of selection bias, errors or incomplete information. The definition of a successful treatment outcome was not consistent across studies and infection control estimates were extracted as reported by the included studies, which could have introduced the possibility of biases in the estimates. This is particularly important because persistence of infection requiring a further DAIR may be considered as a failure in some studies, whereas repeat DAIR is actually part of the treatment protocol in some centres and not considered a failure.(65) Another major limitation was that majority of studies did not make it clear whether DAIR was performed with or without modular exchange, making it impossible to take this into account in our analyses. In one of the largest studies reporting treatment outcomes following the DAIR procedure in hip PJI, exchanging the modular components was reported to be associated with about a 4-fold chance of infection eradication.(65) We were also unable to assess infection control rates across other relevant clinical characteristics such as sex, comorbidities, and whether single or repeat DAIR procedures were performed in patients, because of the lack of appropriate data in contributing studies. Given the substantial heterogeneity among the contributing studies, it was arguable whether a summary estimate should be presented. However, in addition to the summary estimate, we have also reported estimates for relevant subgroups, some of which explained the heterogeneity in our findings. Finally, we were unable to report other outcomes relevant to PJI treatment such as patient function, treatment-associated complications, and quality of life, as these were either not reported by contributing studies or there was lack of consistent reporting.

Conclusions

The overall evidence suggests that the DAIR approach is an effective option for the treatment of PJI in the majority of cases. DAIR is particularly efficacious in treating acute postoperative infections; infections of the hip and shoulder joints; as well as with a shorter duration of parenteral antibiotics after the procedure. Given that DAIR has advantages such as the potential for patients to return quickly to acceptable functional activity, lower morbidity, is well tolerated, and costs less for the health system, its use should be considered in the treatment of PJI.

Conflict of interest

None.

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Figure Legends

Figure 1. Selection of studies included in the meta-analysis

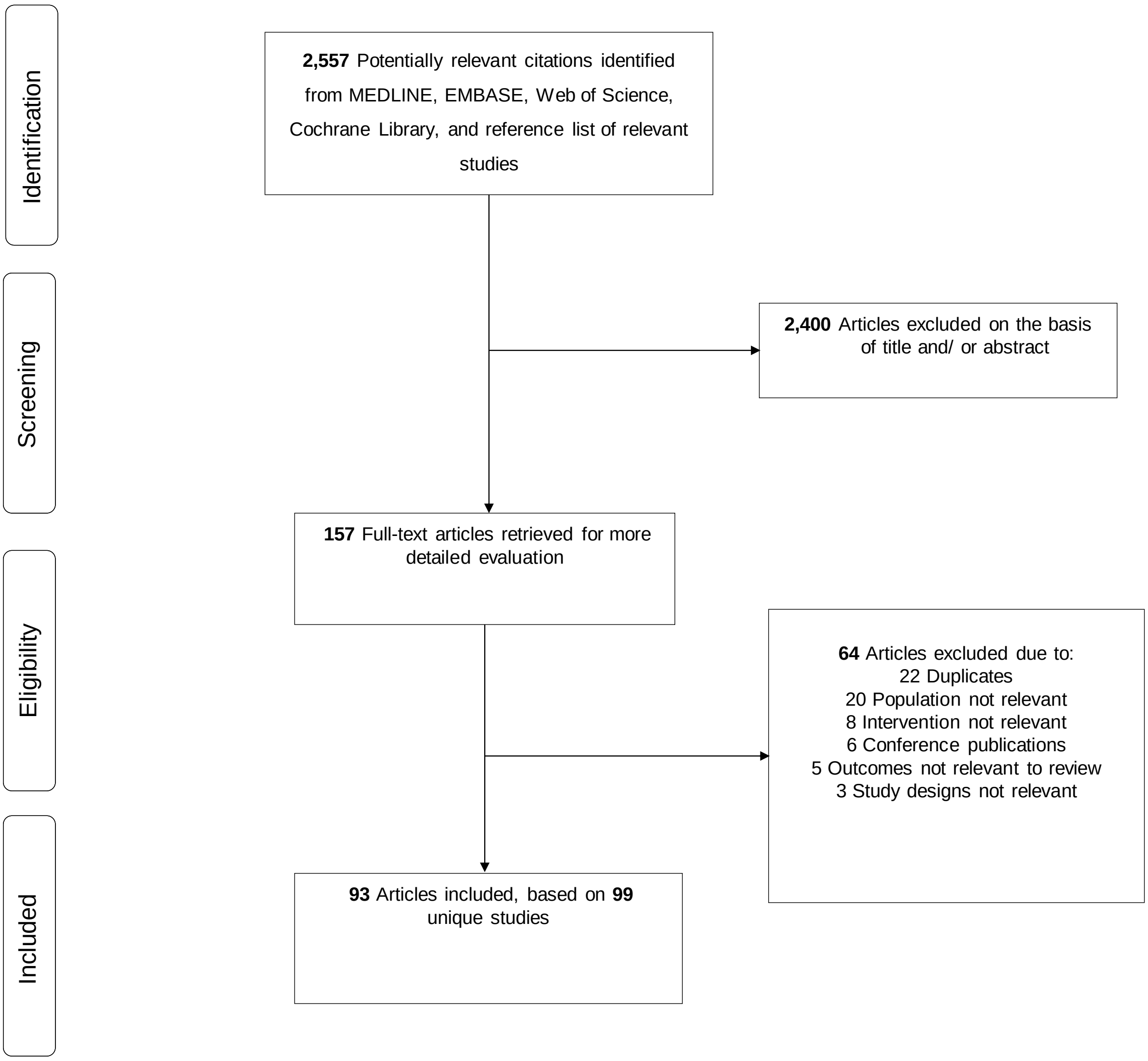
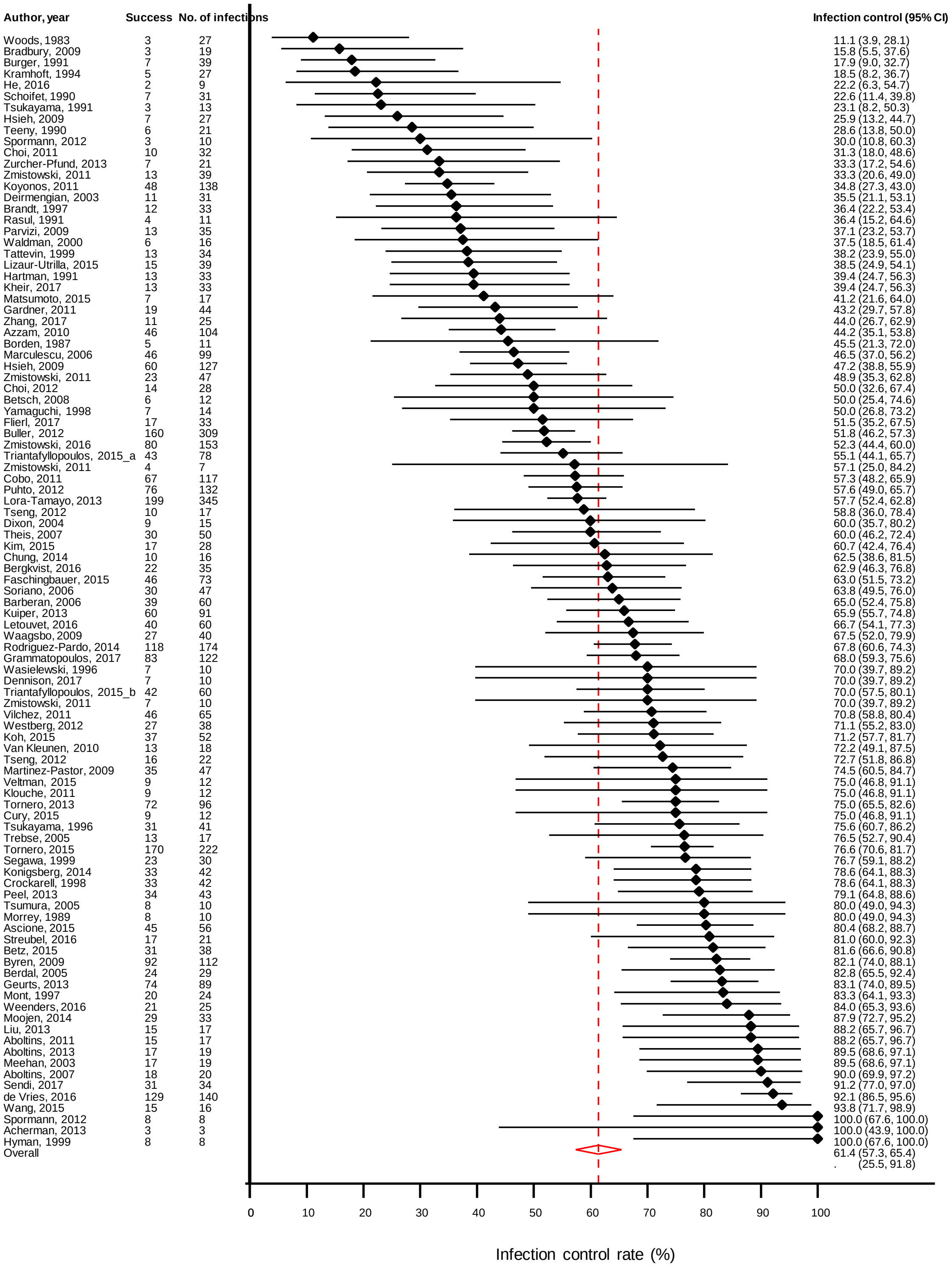


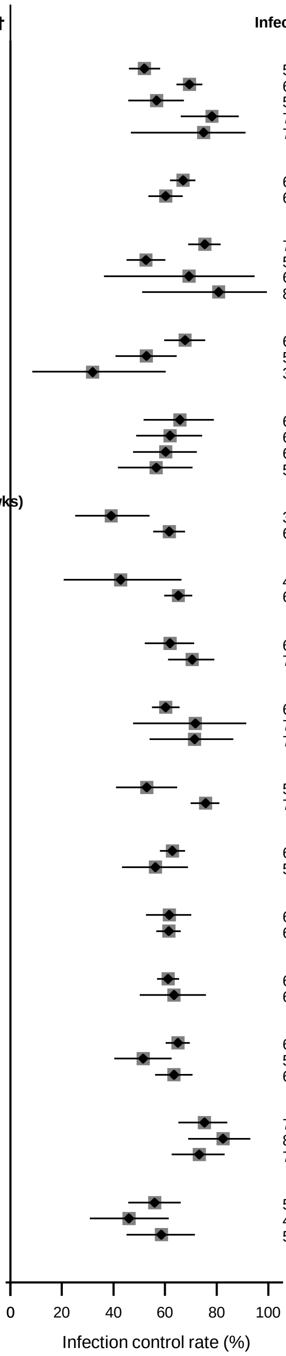
Figure 2. Infection control rates in eligible studies



The summary estimates presented were calculated using random effects models; CI, confidence interval (bars)

Figure 3. Infection control rates in eligible studies, grouped according to several study level characteristics

Subgroup	Infections Controlled†	Total†	Infection control (95% CI)	*P*-value*
Location				
North America	917	1,839	52.00 (46.00, 58.10)	< 0.001
Europe	1,724	2,515	69.50 (64.30, 74.50)	
Asia	200	367	56.70 (45.70, 67.30)	
Pacific	123	164	78.20 (66.00, 88.50)	
South America	9	12	75.00 (46.80, 91.10)	
Average age (years)				
≥ 70	1,354	2,076	67.00 (62.00, 71.80)	0.022
< 70	959	1,735	60.20 (53.50, 66.80)	
Joint type				
Hip	725	996	75.40 (68.90, 81.50)	< 0.001
Knee	629	1217	52.60 (45.10, 60.10)	
Elbow	35	53	69.30 (36.30, 94.70)	
Shoulder	10	13	80.70 (51.10, 99.50)	
Type of infection				
Acute postoperative	657	1037	67.70 (59.60, 75.50)	0.012
Acute haematogenous	123	234	52.70 (40.80, 64.50)	
Late chronic	43	119	31.90 (8.50, 60.20)	
Specific infecting organisms				
Gram negative	201	304	65.80 (51.60, 78.90)	0.905
Gram positive	269	461	62.00 (48.80, 74.30)	
MRSA	37	62	60.20 (47.50, 72.30)	
Staph. Aureus	257	443	56.50 (41.70, 70.70)	
Time from index surgery to symptoms onset (wks)				
> 12	18	46	39.10 (25.10, 53.90)	0.165
≤ 12	299	496	61.70 (55.40, 67.80)	
Duration of symptoms to DAIR (dys)				
≥ 21	228	393	42.80 (20.70, 66.40)	0.071
< 21	1141	1,832	65.10 (59.60, 70.50)	
Time from index surgery to DAIR (dys)				
> 60	359	605	61.90 (52.10, 71.30)	0.206
≤ 60	359	531	70.50 (61.10, 79.10)	
Type of debridement				
Open	1,601	2,712	60.30 (54.90, 65.60)	0.170
Arthroscopic	48	72	71.80 (47.50, 91.40)	
Open or arthroscopic	312	408	71.50 (53.90, 86.40)	
Duration of parenteral ATBs (dys)				
> 14	359	699	52.90 (41.00, 64.70)	0.01
≤ 14	211	281	75.70 (69.90, 81.10)	
Duration of follow-up (yrs)				
> 2	1,868	3,107	62.80 (57.90, 67.70)	0.602
≤ 2	489	808	56.30 (43.30, 68.80)	
No. of participants				
> 100	1,328	2,195	61.60 (52.60, 70.20)	0.938
≤ 100	1,645	2,702	61.40 (56.60, 66.10)	
Quality score				
≥ 12	2,686	4,403	61.20 (56.90, 65.40)	0.831
< 12	287	494	63.40 (50.10, 75.90)	
Period of DAIR procedure (overall)				
≥ 2000	1338	2113	65.00 (60.30, 69.60)	0.028
< 2000	301	618	51.50 (40.40, 62.50)	
Both 90's and 2000+	1304	2073	63.50 (56.10, 70.60)	
Period of DAIR procedure for hip PJI				
≥ 2000	246	346	75.20 (65.20, 84.10)	0.788
< 2000	72	91	82.40 (68.90, 93.00)	
Both 90's and 2000+	407	559	73.30 (62.50, 83.00)	
Period of DAIR procedure for knee PJI				
≥ 2000	212	377	56.00 (45.70, 66.10)	0.261
< 2000	125	299	46.00 (30.90, 61.50)	
Both 90's and 2000+	286	525	58.60 (45.10, 71.50)	



The summary estimates presented were calculated using random effects models; ATBs, antibiotics; CI, confidence interval (bars); DAIR, debridement, antibiotics and implant retention; *, *P*-value for meta-regression; †, total numbers for the subgroups do not add up to the overall total because of missing data in some studies

Table 1. Summary Characteristics of Included Studies Comprising of Participants With PJI and Treated With DAIR

Characteristics	
Participants	**N participants or infections**
Total number that achieved infection control	2,973
Total number of patients or infections	4,897
Study characteristics	
Location	N studies (N participants or infections)
North America	40 (1,839)
Europe	36 (2,515)
Asia	10 (367)
Pacific	6 (164)
South America	1 (12)
Study design	N studies
Retrospective cohorts	82
Prospective cohorts	11
Mean (SD) follow-up (years)	3.6 (1.5)
Study level participant characteristics	
Mean (SD) age, years	68.1 (6.0)
Median (IQR) males, %	46 (38-52)
Joint type*	N participants or infections
Hip and knee	2,387
Knee	1,217
Hip	996
Hip, knee, shoulder, and elbow	174
Elbow	53
Shoulders	13
Hip, knee, and elbow	12
Characteristics of infection and procedure	
Median (IQR) time from index surgery to onset of symptoms, weeks	11.3 (4.0-104.3)
Median (IQR) time from index surgery to infection diagnosis, days	19.5 (16.4-495.7)
Median (IQR) time from index surgery to DAIR, days	91.7 (25.0-520.1)
Median (IQR) time from onset of symptoms to DAIR, days	8.4 (5.0-13.7)
Median (IQR) duration of parenteral antibiotics after DAIR, days	28 (14-37)
Specific infecting organism as reported in the eligible studies*	N participants or infections
Staphylococcus aureus	443
Gram negative	292
Gram positive	180
Staphylococcus species	176
Methicillin resistant Staphylococcus aureus	62
Methicillin resistant Gram positive	47
Methicillin sensitive Gram positive	39
Streptococcus	19

Pseudomonas aeruginosa	12
Mixed polymicrobial	7
Infection type*	N participants or infections
Acute postoperative	1,037
Acute haematogenous	234
Late chronic	119
Debridement type*	N participants or infections
Open	2,712
Arthroscopic or open	408
Arthroscopic	72
Mean (range) of study quality	12 (10-14)

DAIR, debridement, antibiotics and implant retention; IQR=interquartile range; N, number; PJI, periprosthetic joint infection; SD, standard deviation; *, do not add up to the total number of participants or infections as some studies did not report these data